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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,962	09/08/2003	Mendy S. Maccabee	49321-008US0	3139

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1628	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/658,962	MACCABEE ET AL.	
	Examiner	Art Unit	
	JENNIFER M. KIM	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/25/2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 6-8, 21 and 24-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-8,21 and 24-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed June 25, 2010 have been received and entered into the application.

Response to Arguments

Applicants' arguments filed June 25, 2010 have been fully considered but they are not persuasive. Applicants argue that the cited references, alone or in combination, lack disclosure of newly amended limitations because claim 1 has been amended to recite that the vitamin A composition is topically delivered to a sinus cavity from an implant placed in the sinus cavity. This is not persuasive because the topical delivery of vitamin A via implant delivery is obvious in view of Belloni who teach that the depot preparation of vitamin A and that vitamin A can be administered by implantation (column 10, lines 35-45) is old and well known. The selection of pharmaceutical forms, e.g., implants, depot, etc; mode of administration such as topical, transmucosal are all deemed obvious since they are all within the knowledge of the skilled pharmacologist and represent formulations and modes of administration well known in view of Belloni. Applicants argue that Shigeyama discusses only systemic administration of Vitamin A by intramuscular injection, therefore, it is not analogues to topical administration which have different dosage absorption, distribution and elimination profiles. This is not

persuasive because selecting route of administrations of an active agent from those which are already known in the art is a design choice and a preference by the user without surprising and unexpected results. In this case, no unobviousness is seen in the route of administration and the preparation claimed because such are well known route of administration and the preparation formulation of vitamin A in view of Belloni. Applicants argue that Biesalski only discusses aerosol delivery of retinoic acid to the mucosa of the nose-throat cavity and Belloni and Popp fail to cure the deficiencies. This is not persuasive because Biesalski teaches the topical administration of vitamin A compound on the mucosal diseases involving mucosa membrane while Belloni teaches the route of administration and formulations of vitamin A compound depot and implantation of buccal or transmucosal route. Popp et al. teach the therapeutic benefit of vitamin A as an enhancer of wound repair. Therefore, the claimed invention, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 6-8, 21 and 24-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shigeyama (Vitamin A metabolism in nasal and paranasal disease, 1968) in view of Biesalski (U.S.Patent No. 5,556,611) of record, Belloni (U.S.Patent No. 6,339,107 B1) of record and Popp et al. (1995) and further in view of Heiber et al. (U.S.Patent No. 5,766,620).

Shigeyama teaches that inadequate nutrition especially deficiencies in nutrients such as vitamins A and D is the cause of chronic paranasal sinusitis. Shigeyama teaches that vitamin A has a prophylactic effect, and giving vitamins A and D to infants suffering from **paranasal sinusitis** had a curing effect in light cases. (page first full paragraph 34-35). Shigeyama teaches that vitamin A plays an important role in maintaining the function of mucosal epithelia. Shigeyama teaches that the patients having **chronic paranasal sinusitis** were injected with water-soluble **vitamin A** palmitate (Chokola A) by intramuscular injection. Shigeyama teaches that vitamin A is mainly distributed in the epithelial layer, gland tissue and vessels. Shigeyama teaches that their findings revealed that serum vitamin A decreased in chronic paranasal sinusitis patients, suggesting that reduced vitamin A levels caused local regressive changes in mucosa that facilitated infection, and exerted a steady influence on the autonomic nervous system that facilitated allergic changes. These findings also suggest that poor circulation formed between decreased vitamin A and local lesions and also liver function, which simultaneously acted causally to partially inhibit curing and

foster development of a chronic condition. (pages 37 first paragraph, 40, 41, 58, 79 first full paragraph,101).

Shigeyama does not expressly teach topical delivery to sinus cavity, an implant formulations set forth in claims 1 and 6 and the subject had undergone a surgery set forth in claim 27.

Biesalski teaches a pharmaceutical preparation consisting of **retinoic acid** as an active substance suitable for **a topical** treatment of **mucosal disease** in man and animal. (abstract). Biesalski teaches the preparation can be formulated in an **aerosol** formulation. (abstract). Biesalski teaches the effective amount of the active substance is from **0.01-50% by weight**. (column 6, line 44). This range encompasses and touches Applicants' amounts set forth in claim 8. Biesalski teaches that the preparation is effective for treating **functional impairments in the mucous membranes** of humans and animals, in particular in the respiratory epithelium and the epithelia of the **nose-throat cavity**. Biesalski teaches that the treatment is also useful in **reduced activity of the ciliated epithelium** and disturbances of the mucous membranes of the respiratory tract. (column 10, lines 24-45). Biesalski teaches the preparation is effective for treating acute and chronic bronchitis, acute and chronic functional disturbances due to impairment of tracheobronchial epithelium and bronchopulmonary dysplasia.

Belloni teaches that topical administration of retinoic acid can be formulated as solutions, gels, ointments, creams, suspension, etc. as are well-known in the art. (column 8, lines 14-17). Belloni teaches that retinoic acid can be formulated for oral liquid preparations such as suspensions, elixirs and solutions, as well as **transmucosal**

and **buccal** administration. (column 8, lines 35-40, line 40-65, column 9, lines 1-6). Belloni teaches that retinoic acid can be formulated as a **depot preparation and can be administered by implantation**. (column 10, lines 35-45).

Popp et al. teach that it has been known for decades that vitamin A and its derivatives can enhance various aspects of wound repair. (page 46, left-hand side, first paragraph).

Heiber et al. teach that transmucosal delivery system includes a patch (column 11, lines 35-45).

It would have been obvious to one of ordinary skill in the art to employ Vitamin A for the treatment of sinus disease such as paranasal sinusitis or promoting sinus wound healing in a subject because Shigeyama teaches that vitamin A is useful as a prophylactic agent for curing paranasal sinusitis and because vitamin A is known for decades for its enhancement on various aspect of wound repair as taught by Popp et al. One would have been motivated to make such a modification in order to achieve an effective therapeutic benefit of vitamin A in treatment of paranasal sinusitis caused by lack of vitamin A as taught by Shigeyama.

It would have been obvious to one of ordinary skill in the art to administer effective amount of vitamin A via topical delivery including an implant to sinus cavity of the subject having sinus disease or sinus wound because the effective amounts and the topical formulation of vitamin A including an implant for the treatment of disorders related to functional impairments in the mucous membrane and epithelium and the epithelia of nose-throat cavity and paranasal sinusitis is well taught by Shigeyama as

modified by Biesalski and Belloni. It would have been obvious to one of ordinary skill in the art that the topical delivery of vitamin A formulation including an implant taught by Biesalski and Belloni would absorb or penetrate to paranasal cavity in the treatment of paranasal sinusitis in Shigeyama's patients because the amounts and the formulations of vitamin A taught by Biesalski and Belloni are the same topical formulations as instantly claimed. Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. The prior art teaches the identical chemical structure, therefore, the properties applicant discloses and/or claims (topically delivering to sinus cavity) are necessarily present. The limitation of a patch in claim 6 is noted. However, such is obvious in view Heiber et al. who teach that the transmucosal delivery system generally includes a patch.

It would have been obvious to one of ordinary skill in the art to employ retinoic acid preparation taught by Shigeyama as modified by Biesalski and Belloni and Popp et al for the treatment of any sinus wound healing associated with ciliated epithelium healing or ciliated mucosa including any cause of such damage including the specific sinus surgery set forth in claim 27 because both Shigeyama and Biesalski et al teach that the retinoic acid preparation is effective for the treatment of impaired ciliated epithelium and disturbances of the mucous membranes in general including **paranasal sinusitis** and that Popp et al. teaches the wound healing effect of tretinoin (retinoic acid) was known at the time the invention was made. One would have been motivated to employ the retinoic acid preparation in the methods taught by Shigeyama as modified by Biesalski, Belloni and Popp et al. for a condition of damaged ciliated epithelium or a

condition of disturbances of the mucous membranes at any cause including the surgical intervention in order to effectively treat the condition and obtain the known wound healing effect of retinoic acid. There is a reasonable expectation of successfully treating damaged ciliated epithelium in **paranasal sinusitis** because cited references Shigeyama, Biesalski, and Belloni teach the effectiveness of vitamin A for treating damaged ciliated epithelium or damaged respiratory walls in man or animal including paranasal sinusitis and its well known would healing effect.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER M. KIM whose telephone number is (571)272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JENNIFER M KIM/
Primary Examiner, Art Unit 1628

Jmk
August 3, 2010